

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-61 (canceled)

Claim 62 (currently amended) A method for producing a non-human transgenic animal, the method comprising:

- (a) modifying the nuclear genome of a somatic cell with a normal karyotype at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of the somatic cell to an oocyte, two cell embryo or zygote ~~recipient cell~~ to produce a nuclear transfer unit;
- (c) activating the nuclear transfer unit thereby producing an animal embryo;
- (d) transferring the embryo to a surrogate mother; and
- (e) allowing the animal embryo to develop to term, thereby producing a non-human transgenic animal.

Claim 63 (previously presented) The method of claim 62, wherein the transgenic animal is a transgenic sheep, cow, bull, goat, pig, horse, camel, rabbit or rodent.

Claim 64 (previously presented) The method of claim 62, wherein the genetic targeting event is mediated by homologous recombination.

Claim 65 (previously presented) The method of claim 62, wherein the genetic targeting event results in removal of a gene, modification of a gene, upregulation of a gene, gene replacement or transgene placement.

Claim 66 (previously presented) The method of claim 62, wherein the genetic targeting event results in inactivation of a gene.

Claim 67 (previously presented) The method of claim 62, wherein the genetic targeting event results in a gene targeted cell clone: randomly targeted cell clone ratio of equal to or greater than 1:100.

Claim 68 (canceled)

Claim 69 (canceled)

Claim 70 (previously presented) The method of claim 62, wherein the modification comprises placing a promoter adjacent to an endogenous gene in the nuclear genome.

Claim 71 (previously presented) The method of claim 70, wherein the promoter is a collagen gene promoter.

Claim 72 (previously presented) The method of claim 70, wherein the promoter is a milk protein gene promoter.

Claim 73 (currently amended) The method of claim 70, wherein the promoter directs ~~abundant~~ expression of at least one gene in fibroblast cells.

Claim 74 (canceled)

Claim 75 (previously presented) The method of claim 62, wherein the modification comprises placing a marker gene at the endogenous locus in the nuclear genome.

Claim 76 (previously presented) The method of claim 75, wherein the marker gene is a gene that confers resistance to a drug.

Claim 77 (previously presented) The method of claim 76, wherein the gene that confers resistance to a drug is selected from the group consisting of neomycin, G418, hygromycin, zeocin, blasticidin and histidinol.

Claim 78 (previously presented) The method of claim 75, wherein the marker gene is selected from the group consisting of HPRT, gpt, a visible marker gene and a gene that can be detected with a single chain antibody/hapten system.

Claim 79 (previously presented) The method of claim 78, wherein the visible marker gene is GFP.

Claim 80 (previously presented) The method of claim 62, wherein the modification comprises removing a negatively selectable marker gene.

Claim 81 (previously presented) The method of claim 80, wherein the negatively selectable marker gene is a toxin gene.

Claim 82 (previously presented) The method of claim 62, wherein the genetic targeting event is mediated by lipofection.

Claim 83 (previously presented) The method of claim 62, wherein the genetic targeting event comprises the use of a gene targeting vector, which vector comprises a region of homology to a target locus.

Claim 84 (previously presented) The method of claim 83, wherein the region of homology is greater than 7 kb in length.

Claim 85 (previously presented) The method of claim 62, wherein the genetic targeting event comprises the use of a gene targeting vector which is in a circular form.

Claim 86 (previously presented) The method of claim 62, wherein the somatic cell is a primary somatic cell.

Claim 87 (previously presented) The method of claim 62, wherein the somatic cell is an epithelial cell, a fibroblast cell, an endothelial cell or a muscle cell.

Claim 88 (previously presented) The method of claim 62, wherein the somatic cell is a G₀ cell.

Claim 89 (previously presented) The method of claim 88, wherein the G₀ cell is obtained by serum starvation of a somatic cell.

Claim 90 (currently amended) A method for producing transgenic offspring from a transgenic animal, the method comprising:

- (a) modifying the nuclear genome of a somatic cell with a normal karyotype at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of the somatic cell to a an oocyte, two cell embryo or zygote recipient cell to produce a nuclear transfer unit;
- (c) activating the nuclear transfer unit thereby producing an animal embryo;
- (d) transferring the embryo to a surrogate mother;
- (e) allowing the animal embryo to develop to term, thereby producing a non-human transgenic animal; and.
- (f) breeding the transgenic animal to produce transgenic offspring from the transgenic animal.

Claims 91- 97 (canceled)

Claim 98 (previously presented) The method of claim 90, wherein the genetic targeting event is mediated by homologous recombination.

Claim 99 (previously presented) The method of claim 90, wherein the genetic targeting event results in removal of a gene, modification of a gene, upregulation of a gene, gene replacement or transgene placement.

Claim 100 (previously presented) The method of claim 90, wherein the genetic targeting event results in inactivation of a gene.

Claim 101 (canceled)

Claim 102 (previously presented) The method of claim 90, wherein the modification comprises placing a promoter adjacent to an endogenous gene in the nuclear genome.

Claim 103 (previously presented) The method of claim 102, wherein the promoter is a collagen gene promoter.

Claim 104 (previously presented) The method of claim 102, wherein the promoter is a milk protein gene promoter.

Claim 105 (currently amended) The method of claim 102, wherein the promoter directs ~~abundant~~ expression of at least one gene in fibroblast cells.

Claim 106 (previously presented) The method of claim 90, wherein the modification comprises placing a marker gene at the endogenous locus in the nuclear genome.

Claim 107 (previously presented) The method of claim 106, wherein the marker gene is a gene that confers resistance to a drug.

Claim 108 (previously presented) The method of claim 107, wherein the gene that confers resistance to a drug is selected from the group consisting of neomycin, G418, hygromycin, zeocin, blasticidin and histidinol.

Claim 109 (previously presented) The method of claim 106, wherein the marker gene is selected from the group consisting of HPRT, gpt, a visible marker gene and a gene that can be detected with a single chain antibody/hapten system.

Claim 110 (previously presented) The method of claim 109, wherein the visible marker gene is GFP.

Claim 111 (previously presented) The method of claim 90, wherein the modification comprises removing a negatively selectable marker gene.

Claim 112 (previously presented) The method of claim 111, wherein the negatively selectable marker gene is a toxin gene.

Claim 113 (previously presented) The method of claim 90, wherein the genetic targeting event is mediated by lipofection.

Claim 114 (previously presented) The method of claim 90, wherein the genetic targeting event comprises the use of a gene targeting vector, which vector comprises a region of homology to a target locus.

Claim 115 (previously presented) The method of claim 114, wherein the region of homology is greater than 7 kb in length.

Claim 116 (previously presented) The method of claim 90, wherein the genetic targeting event comprises the use of a gene targeting vector which is in a circular form.

Claim 117 (previously presented) The method of claim 90, wherein the somatic cell is a primary somatic cell.

Claim 118 (previously presented) The method of claim 90, wherein the somatic cell is an epithelial cell, a fibroblast cell, an endothelial cell or a muscle cell.

Claim 119 (previously presented) The method of claim 90, wherein the somatic cell is a G₀ cell.

Claim 120 (previously presented) The method of claim 119, wherein the G₀ cell is obtained by serum starvation of a somatic cell.

Claim 121 (previously presented) The method of claim 62 or 90, wherein the genetic targeting event is mediated by electroporation.

Claim 122 (previously presented) The method of claim 62 or 90, wherein the genetic targeting event is mediated by transfection.

Claim 123 (previously presented) The method of claim 66, wherein the gene that is inactivated is α -1,3 galactosyltransferase.

Claim 124 (previously presented) The method of claim 99, wherein the gene that is inactivated is α -1,3 galactosyltransferase.

Claim 125 (previously presented) The method of claim 62 or 90, wherein the endogenous locus is an immunoglobulin gene.

Claim 126 (previously presented) The method of claim 123, 124 or 125, wherein the transgenic animal is a pig.

Claim 127 (previously presented) The method of claim 123, 124 or 125, wherein the transgenic animal is a cow.

Claims 128- 130 (canceled)

Claim 131 (currently amended) A method for producing a non-human transgenic animal, the method comprising:

- (a) modifying the nuclear genome of a somatic cell with a normal karyotype at an endogenous locus by a genetic targeting event;
- (b) accomplishing successful nuclear transfer to produce the non-human transgenic animal.

Claim 132 (currently amended) A method for producing a non-human transgenic animal, the method comprising:

- (a) modifying the nuclear genome of a somatic cell with a normal karyotype at an endogenous locus by a genetic targeting event;

- (b) transferring the modified nuclear genome of the somatic cell to an oocyte, two cell embryo or zygote ~~activated recipient cell~~ to produce a nuclear transfer unit;
- (c) transferring the nuclear transfer unit to a surrogate mother; and
- (d) allowing the animal embryo to develop to term, thereby producing a non-human transgenic animal.

Claim 133 (currently amended) A method for producing transgenic offspring from a transgenic animal, the method comprising:

- (a) modifying the nuclear genome of a somatic cell with a normal karyotype at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of the somatic cell to a an oocyte, two cell embryo or zygote ~~recipient cell~~ to produce a nuclear transfer unit;
- (c) activating the nuclear transfer unit thereby producing an animal embryo;
- (d) transferring the embryo to a surrogate mother;
- (e) allowing the animal embryo to mature ~~in a manner that accomplishes breeding~~.